

## **REMARKS**

### **Claim Status**

Claims 1-17 and 21-23 were presented for examination; claims 18-20 were withdrawn earlier. Claims 1-14, 16 and 23 were rejected. Claims 15, 17, 21 and 22 were objected to because they depend from rejected base claim, but would be allowable if rewritten in independent form. Claims 1-17 and 21-23 were rejected as allegedly containing non-elected subject matter. However, the examiner has stated that the scope of the examined subject matter will be expanded upon removal of all art-based rejections. Accordingly, those claims have not been amended.

The Applicants appreciate withdrawal of the previous rejection under 35 USC 112, and withdrawal of the obviousness rejection based on Kuroita, US Patent No. 6,468,998, which relied upon *In re Henze*. In view of that, the only rejection is for obviousness as discussed below.

No claim amendments are made at this time. Reconsideration in view of the following remarks is respectfully requested.

### **Rejections under 35 USC 103**

Claims 1-17 and 21-23 were alleged to be obvious in view of Kuroita, US Patent No. 6,468,998. According to the Examiner, the claims are rendered obvious by a particular compound disclosed in Kuroita at col. 32, lines 5-14 and col. 45, lines 12-21, which corresponds to Example 74. The Examiner alleged that this compound corresponds to the claimed invention where W is L<sup>2</sup>-A<sup>3</sup>; L<sup>1</sup> and L<sup>2</sup> are optionally substituted C<sub>1</sub>-C<sub>5</sub> alkylenes; A<sup>1</sup>, A<sup>2</sup> and A<sup>3</sup> are each phenyl; X<sup>1</sup> is CR<sup>3</sup>; and all other substituents are as defined. The difference between the claims and Kuroita was said to be that Kuroita does not teach "compounds that meet the proviso that L<sup>1</sup> must contain at least three linking atoms if X<sup>1</sup> is CH and W is L<sup>2</sup>-A<sup>3</sup>." The Examiner further alleges that "Hydrogen and methyl are obvious variants. A compound in which methyl is swapped for hydrogen would be expected to have similar properties to the parent molecule. The court in *In re Wood* (199 USPQ 137) states that compounds with similar structures are expected to have similar properties unless

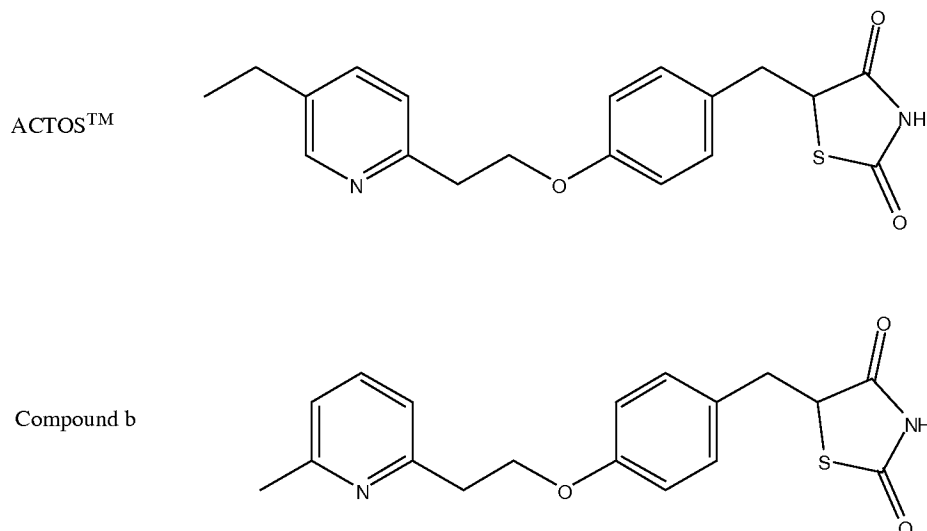
there is evidence on the record of secondary considerations. Therein lies the motivation and a reasonable expectation of success to change X<sup>1</sup> from CH to CCH<sub>3</sub>.”

The Applicants traverse this rejection. The law as it relates to obviousness in chemical inventions is aptly and Very recently discussed in *Takeda v. Alphapharm*, which was decided by the Federal Circuit in an opinion issued on June 28, 2007—after, and specifically referring to the Supreme Court case on obviousness, *KSR v. Teleflex*. In *Takeda*, the court upheld a finding that species and subgenus claims were NOT rendered obvious even though a prior art genus encompassed the species and subgenus and *also* disclosed a species that closely resembled the claimed compound.

*Takeda* arose in a litigation context, but the court’s reasoning was based on a collection of cases having nothing to do with litigation: the *Takeda* court said that no *prima facie* case of obviousness was established under the law on obviousness as it relates to chemical inventions. The court based its obviousness standard on *In re Grabiak*, 226 USPQ 870; *In re Jones*, 21 USPQ2d 1941 (Fed. Cir. 1992); *In re Dillon*, 16 USPQ2d 1897; and *In re Lalu*, 223 USPQ1257 (Fed. Cir. 1984). None of these is a litigation case: they all relate to patent examination appeals, which shows that the standard the court applied in *Takeda* is the ordinary obviousness standard, not a distinct one for litigation.

The compound claimed in *Takeda* was the drug Actos, and the Non-obvious claims also included subgenus claims covering isomers of Actos where the Ethyl group on the pyridine ring could be at any position on the ring. For the Examiner’s convenience, the structures of Actos and the closest species in the prior art, referred to as Compound b, are provided below. Note that despite the very substantial similarity between Compound b and Actos, and differences that are limited to the exact size and location of the alkyl group on the pyridine ring, Actos was not rendered obvious by compound b. Methyl to ethyl is a one-atom homologation; moving the group from position 6 to position 5 seems trivial and remains well within the scope of the prior art genus. Nevertheless, Actos was not obvious because the prior art did not provide motivation to select

compound b as a starting point, and there was nothing in the prior art that provided motivation to make the “specific molecular modifications” needed to arrive at the claimed invention.



The district court in *Takeda* concluded that Alphapharm did not provide a *prima facie* case of obviousness, and even if it had, there was evidence of unexpected results to rebut any *prima facie* case. The Federal Circuit went further: it expressly said that there was no *prima facie* case, so the secondary considerations need not even be considered. *Takeda* at 1179. According to the Federal Circuit, Alphapharm did not provide a Reason to select Compound b from the reference: there was no data or other indication to show that a person of ordinary skill would have selected it as a starting point. Moreover, even if that compound had been properly selected, the Federal Circuit stated that there was nothing in the Prior Art that would have motivated one to make the ‘specific molecular modifications’ needed to arrive at the claimed invention. Thus, even though secondary evidence of nonobviousness was available, it was not necessary to consider it because no *prima facie* case for obviousness had been made out.

The Federal Circuit quoted from *Dillon*, saying that “structural similarity between claimed and prior art subject matter, proved by combining references or otherwise, where the prior art gives reason or motivation to make the claimed compositions, creates a *prima facie* case of obviousness.” But it went on to quote from *In re Grabiak*, 769 F.2d 731-32 (Fed. Cir. 1985), saying

this: “In addition to structural similarity between the compounds, a prima facie case of obviousness also requires a showing of ‘adequate support in the prior art’ for the change in structure.” *Takeda* at 1174. While *In re Deuel* indicates that structural similarity can be the basis for a finding that another structure may have similar properties, that is nonetheless, according to the court in *Takeda*, not enough to provide an obviousness conclusion. There must also be a reason to make the allegedly ‘obvious’ compound without reference to the present invention.

In the present case, like *Takeda*, there is nothing in the prior art that would have led one to select the particular compound that the Examiner used as the basis for the proposed obviousness case. That compound is Example 74: it is one of hundreds of species that the reference disclosed, and the Examiner offers no explanation for selecting it as the starting point. It was selected based on the present disclosure, as the closest structure to the claimed invention. Based on the reference, though, there appears to be no reason for one of ordinary skill to select that species, from the many that were disclosed.

Furthermore, there is nothing in the prior art that suggests making the “specific molecular modifications” to the compound of Example 74 that would be needed to produce a compound within the scope of the present claims. The Examiner alleges that H and Me are ‘obvious variants’. The Applicant traverses that assertion: replacing H with Me is simply not the same as homologating an existing alkyl group. Replacing H with methyl involves adding a substituent where none existed before, and where none was *suggested* before.

Moreover, even if it were true that H renders Me ‘obvious’, though, that is not enough under *Takeda* to support a finding of obviousness, because there is simply no reason why a person of ordinary skill would have chosen to make that change—even if there were a reason to select the species of Example 74 as a starting point. Nothing suggests making this particular modification from among all possibilities, just as nothing in the prior art in *Takeda* suggested moving the methyl group over by one position on the pyridine ring, or homologating it.

Indeed, in *Takeda* the proposed modified structure—Actos, which was NOT obvious—was admittedly within the scope of the prior art genus. In the present case, the modified compound suggested by the Examiner is not within the scope of the prior art genus: the prior art genus does not encompass the modified compound that the Examiner relies upon to allege obviousness. Thus to the extent that one of ordinary skill would have been motivated to modify compounds within the prior art genus, that would not have been enough to produce the modification suggested by the Examiner: the genus in the prior art does not encompass compounds having a methyl group where the Examiner proposed putting one. Thus the prior art does not even provide a reasonable expectation that this modification will maintain activity, since its genus does not cover the modified compound.

As in *Takeda*, this obviousness analysis relies upon the present disclosure to guide the selection of a starting point that would *NOT* have been obvious to a person of ordinary skill before the present invention was made. And, as in *Takeda*, even if only simple modifications would have been required to arrive at the claimed invention, there is simply no reason in the prior art to make the ‘specific molecular modifications’ needed to get to the claimed invention. Nothing in the reference would have suggested replacing H with Me where the Examiner suggested doing that: indeed, that replacement produces a compound outside the scope of the prior art genus. There are hundreds, at least, of changes that could have been made to this or any other species in the prior art; as *Takeda* demonstrates, those modified compounds are not ‘obvious’ in the absence of some reason to make the “specific molecular modifications”.

The cited reference provides no motivation to select the starting point that was required by the present obviousness rejection; and even if it were selected, the prior art provided no reason to modify it as proposed. Accordingly, under the *Takeda* standard, no *prima facie* case for an obviousness rejection has been presented, and this rejection should be withdrawn.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 381092001600. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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